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EXAMINER

CRANE, LAWRENCE E

ART UNIT

PAPER NUMBER

1623

NOTIFICATION DATE

DELIVERY MODE

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ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| | | | |
|------------------------------|--------------------------------------|--------------------------------------|--|
| Office Action Summary | Application No. 10/590,268 | Applicant(s) SEKINE ET AL. | |
| | Examiner Lawrence E. Crane | Art Unit 1623 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on October 22, 2009 (amendment).
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 October 2009 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

The Abstract of the Disclosure is objected to because it does not meet the requirement of the MPEP for US application. Correction is required. See MPEP 608.01(b).

Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts, compounds or compositions, the general nature of the compound or composition should be given as well as its use, e.g., "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary. Complete revision of the content of the abstract is required on a separate sheet.

Examiner notes with appreciation the changes made to the Abstract. Unfortunately, many errors have also found their way into the amended Abstract, including many of the same errors noted in the objections and rejections recited below for similar terminology now found in the claims. Applicant is referred to the objections and rejections below for guidance concerning how the Abstract should be amended in parallel.

Examiner notes with appreciation the submission of a formal drawing. In reviewing the Brief Description of the Drawings in the disclosure at page 4, Examiner respectfully requests that said "Brief Description" be amended to more completely and accurately describe the contents of the Figure. The replacement Figure is considered to have met the previous request for a formal drawing.

No claims have been cancelled, claims **1, 4, 5, 8, 10-12 and 14-16** have been amended, the disclosure has been amended at page 1, the Abstract has been amended, and no new claims have been added as per the amendment filed October 22, 2009. No additional or supplemental Information Disclosure Statements (IDSs) have been filed as of the date of this Office action.

Claims **1-16** remain in the case.

Note to applicant: when a rejection refers to a claim **X** at line **y**, the line number "y" is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

35 U.S.C. §101 reads as follows:

“Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.”

Claims **15 and 16** are rejected under 35 U.S.C. §101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. §101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App., 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149, 149 USPQ 475 (D.D.C. 1966).

Applicant has amended claims **15 and 16** by substitution of an alternative for the term “use” wherein said substitute term is not a derivative or a conjugation of the verb -- to use --. However, applicant’s failure to fully describe the process steps being claimed in effect means that the noted claims remain in effect “use” claims and that said claims remain subject to the same rejection until such time as applicant fills in the blanks by adding sufficient detail to permit a detailed determination of what is included within each of the claimed process steps. Examiner respectfully suggests a much more complete and detailed claim set wherein the chemical structures /identities/definitions of the process starting materials, reagents, critical reaction conditions, intermediates and final products are provided in the claims.

Applicant’s arguments filed October 22, 2009 have been fully considered but they are not persuasive.

Examiner notes with appreciation the deletion of the term “use,” but finds that the other changes are simply inadequate to overcome the basic thrust of the above rejection, said thrust being that the claims remain generic and therefore remain in effect use claims in spite of the deletion of the offending term. Applicant has argued that the amendments of the noted claims now support the assertion that these claims “... recite process steps.” Examiner respectfully disagrees, noting that claim **16** does not yet meet the minimum standard to be considered a valid process claim (see second paragraph analysis below), and that claim **15** is so brief that said claim is at present little more than a compound claim. Applicant is respectfully requested to provide much more complete and detailed descriptions of each and every one of the steps in the claimed process in order to overcome this rejection.

Claims **1-16** are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for a specific process for the derivatization of a “highly cross-linked polystyrene” (aka “HCP”) solid support by reaction of a functional group attached to said HCP possibly with a compound of claim **1** to create a solid support derivatized to serve as the starting point for nucleic acid synthesis, does not reasonably provide enablement for any other process wherein a solid support is derivatized for the indicated synthetic purpose by a compound of claim **1**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of “undue experimentation” is appropriate are as follows:

A. The breadth of the claims is found to greatly exceed the scope of the enabling embodiments because the claims are directed to any solid support derivatized by a compound of claim **1** and the subsequent application of said derivatized solid support as a starting material in a phosphoramidite-type oligonucleotide synthesis process.

B. The nature of the invention: This subject matter was described in the previous paragraph.

C. The state of the prior art: A present there is no prior art of record that anticipates or renders obvious the instant claimed subject matter.

D. The level of one of ordinary skill: One of ordinary skill would be expected to be knowledgeable concerning organic synthesis and the synthesis of derivatized solid support with utility in the synthesis of oligonucleotides.

E. The level of predictability in the art: In view of the confused and incomplete nature of the subject matter as presently of record in the instant claims, it is presently not possible to determine the predictability for the entire scope of the subject matter, particularly when referring to the compounds of indeterminate structure referred to in claim **1** and some claims dependent therefrom

F. The amount of direction provided by the inventor: The instant disclosure provide less than 14 pages most of which is devoted to the description of how to make synthetic precursors. The disclosure at pages 17-19 only includes one operational set of embodiments to enable the claimed synthesis-capable solid support and its application to the syntheses of an oligoadenylate and an oligothymidylate. .

G. The existence of working examples: This subject matter was described in the previous paragraph.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is found to be excessive because of the indefiniteness and ill defined metes and bounds of the claims as presently in the case, and because of what appears to be a scope of claimed subject matter that is not adequately enabled by the very small number of specific embodiments.

Applicant's arguments filed October 22, 2009 have been fully considered but they are not persuasive.

Applicant argues that the instant claim set now adequately defines the chemical actors intended to be claimed and the method claims directed to using same to make oligonucleotides. Examiner respectfully disagrees, noting the numerous new grounds of rejection listed below wherein the indefiniteness of the claims is noted in detail. In view of the continuing indefiniteness of the claims even after amendment, and the consequential difficulty of determining whether the scope of the claims is adequately enabled, examiner respectfully disagrees with applicant's conclusion and therefore has maintained the instant grounds of rejection.

The disclosure is objected to because of the following informalities:

Applicant is referred to the comments *in re* the Abstract made supra and respectfully requests similar amendments to the disclosure as appropriate to insure that there is consistency in the numerical subscript notations present therein identifying defined structural variables.

Appropriate correction is required.

Claims **1-3, 6, 7 and 12** are objected to because of the following informalities:

In claim **1** at line 4, the variables are uniformly provided with subscript numbers (e.g. “R₁”), but the remainder of the claim fails to provide similar subscripted numbers following the various variables “RX” wherein X = 1-5. Applicant is respectfully requested to amend the non-subscripted variables to be consistent with the variables provided in the generic formula. See also claims **2, 3, 6, 7 and 12** wherein the same inconsistencies reoccur.

Appropriate correction is required.

Claims **1-16** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim **1** at line 1, the term “3’-end nucleoside unit comprising phosphoramidite that is a compound represented by the following formula:” has internally inconsistent definitions of the metes and bounds of the claimed subject matter because the term “comprising” is open language suggesting that only part of said chemical “formula” is presented in the claim, while the term “a compound represented by the following formula” requires a closed or limited-by-the-structure-provided definition of what is being claimed (terminology claiming broad scope of subject matter coverage and narrow scope of subject matter coverage in the same claim is a well known type of indefiniteness: see form paragraph 7.34.04 in the MPEP). Applicant is respectfully requested to amend the noted term to limit the subject matter to the provided formula. See also claim **12** for the same or similar errors.

Applicant’s arguments with respect to claims **1-16** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant’s amendments.

In claim **1** at lines 4 and 6, the chemical structural formula wherein a line representing a bond to a furanose ring ends with the notation “ 5’ ” is not further defined in the subsequent claim. In view of the root names provided in claims **10 and 11** (“thymidine” and “2’-deoxyadenosine”) examiner guesses that the term “ -5’ ” may have been intended to be defined as -- HO-H₂C- --. See also claim **12** wherein the same or similar errors reoccur.

Applicant’s arguments with respect to claims **1-16** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant’s amendments.

In claim **1** at line 4, the term “-(C₆H₄)-” does not provide for the possibility of benzene ring substitution, and thereby causes dependent claims wherein this possibility is introduced to lack adequate antecedent basis. In order to address this issue directly, examiner respectfully suggests amendment of the noted term to read -- -(C₆H₃R₆)- -- with added definition of the new variable R₆ in claim **1** (e.g. -- R₆ is lower alkyl, halo, nitro, cyano, or methoxyl --) Cancellation of claim **8** and amendments introducing the new variable and the more narrowly defined metes and bounds thereof {possibly introduce -- R₆ is C₁₋₄ alkyl, halo, nitro, cyano, or methoxyl -- into claim **9**} would also be required to complete the introduction of the new variable into the claim set and permit claim **9** to be further limiting of the scope of claim **1** and therefore properly dependent. Appropriate amendments are respectfully requested. See also claim **12** wherein the same or similar errors reoccur.

Applicant's arguments with respect to claims **1-16** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

In claim **1** at line 6, the term “a nucleoside or its derivative” is indefinite for failure to define the metes and bounds of the included term “derivative,” and is inaccurate because, in view of the generic formulas provided in claim **1**, the only nucleosides that may be considered are -- 2'-deoxyribonucleosides --. Examiner respectfully suggests that the noted term may be amended to read -- a 2'-deoxyribonucleoside or its N-protected derivative --. See also claim **12** at line 5 wherein the same error reoccurs.

Applicant's arguments with respect to claims **1-16** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

In claim **1** at line 6, the following the term “derivative,” examiner respectfully suggests introduction of the following term in order to make the claim more grammatical:
-- wherein the substituent --.

Applicant's arguments with respect to claims **1-16** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

In claim **1** at line 7, the term “a sugar of the nucleoside” is grammatically and technically erroneous and should be amended to read -- the sugar moiety of the nucleoside substituent --, or the like. See also claim **12** wherein the same or similar errors reoccur.

Applicant's arguments with respect to claims **1-16** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

In claim **1** at line 8, the term “aryl group” is incomplete and therefore causes a lack of antecedent basis in claim **3**. In order to address this problem, examiner respectfully suggests that the noted term should be amended to read -- optionally substituted aryl group -- and that in addition the possible substituents (see claim **3**) should be defined (possibly more generically) in claim **1**. If claim **3** is entirely incorporated into claim **1**, then claim **3** should be cancelled or other appropriate measures taken to avoid a failure of claim **3** to further limit the scope of independent claim **1**.

Applicant's arguments with respect to claims **1-16** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

Examiner respectfully suggests that claim **3** may be replaced in its entirety by the following:

-- **3**. The compound according to claim **1** wherein R_1 and R_2 are independently substituted aryl wherein the substituent is selected from the group consisting of alkyl, nitro, cyano, halo and methoxyl. -- .

Applicant is advised that changes to claim **1** may make this suggestion inappropriate if the scope of claim **1** is not further limited.

Applicant's arguments with respect to claims **1-16** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

In claim **4** at line 3, the term “group” is superfluous and should be deleted.

Applicant's arguments with respect to claims **1-16** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

Examiner respectfully suggests that claim **6** should be replaced in its entirety by the following:

-- **6**. The compound according to claim **1** wherein each of R₄ and R₅ is independently C₁₋₄ alkyl, benzyl, phenyl or naphthyl. --.

The suggested changes make the claim more grammatical and also shorter.

Applicant's arguments with respect to claims **1-16** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

Examiner respectfully suggests that claim **7** should be replaced in its entirety by the following:

-- **7**. The compound according to claim **1** wherein each of R₄ and R₅ is independently isopropyl. -- .

The proposed change makes the noted claim more grammatical and improves clarity.

Applicant's arguments with respect to claims **1-16** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

Examiner respectfully suggests that claim **9** should be replaced in its entirety by the following:

-- **9**. The compound according to claim **1** wherein the R₆ substituent of the benzene ring structure -(C₆H₃R₆)- is selected from the group consisting of C₁₋₄ alkyl, halo, nitro, cyano and methoxyl. -- .

The suggested changes in claim **9** are in parallel with the changes already suggested for claim **1**.

Applicant's arguments with respect to claims **1-16** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

In claims **10 and 11**, the newly added term "having the structure" is incorrect because no chemical structure has been supplied as part of either claim. In addition, the names supplied are incorrect; e.g. the position of the benzyl group in the structures of claims **1 and 12** is asymmetric, but the name does not appear to specify the attachments thereof unequivocally, etc. Examiner respectfully suggests introduction of complete chemical structures and concomitant deletion of the names as one effective way to insure that the subject matter intended to be claimed is in fact being claimed.

Applicant's arguments with respect to claims **1-16** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

In claim **12** at line 3, the term "the following formula" should be amended to read -- formula II -- in order for the references to formula II at lines 3 and 5 to be consistent, thereby avoiding confusion.

Applicant's arguments with respect to claims **1-16** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

In claim **13** at lines 12, the term "nucleoside unit at a ratio of" was amended to read -- nucleoside units **present** at a ratio of -- (emphasis added only to highlight changes) .

The change is suggested to insure clarity in the definition of claimed subject matter.

Applicant's arguments with respect to claims **1-16** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

Claim **8** asserts that "a benzene ring structure has a substituent," and thereby fails to further limit the scope of the claim depended from. Examiner suggests that claims **8 and 9** may be referring to an --additional substituent --.

Applicant's arguments filed October 22, 2009 have been fully considered but they are not persuasive.

Examiner notes with appreciation applicant's amendment, but for the reasons of record above *in re* claims **8 and 9**, the instant claims are found to remain indefinite. Therefore, the above rejection has been maintained. See new grounds of rejection above and the suggestion that claim **8** may be cancelled if the subject matter of said claim has been incorporated into claim **1**.

Claim **12** is directed to a complex chemical structure only a few structural elements of which have been described thereby rendering the claim incomplete. Claims **13 and 14** add some details but not enough detail to overcome the problem with claim **12** even if incorporated within claim **12**.

Applicant's arguments filed October 22, 2009 have been fully considered but they are not persuasive.

Applicants argue that claim **12** as amended is now complete. Examiner respectfully disagrees, noting that various specific flaws have been listed in rejections of newly amended claim **12**, rejections that are now found above. Examiner respectfully suggests that substantial additional amendments of claim **12** remain in order herein.

Claims **15 and 16** are incomplete because both claims either independently, taken together, or taken in sum with claim **12**, fail to fully describe the process step or steps being claimed, let alone the chemical starting materials and reagents necessary to carry out the claimed process of oligonucleotide synthesis.

Applicant's arguments filed October 22, 2009 have been fully considered but they are not persuasive.

As noted in the 101 rejection above, the amendments to claim **15** have not introduced any process step limitations. The term "comprising synthesizing a nucleic acid oligomer" is entirely functional and provides no effective chemical process step limitations whatsoever. Additionally, claim **16** remains incomplete as a process claim at best because the newly amended limitations continue to lack the detail necessary to permit an ordinary practitioner to determine the metes and bounds of the claimed process steps. For example, the noted claim

has not identified with particularity the “activating agent(s),” provided the specific identities of the “alcohol-type compound,” or listed the particular “acid catalysts” implied by said incompletely defined generic terms. Examiner respectfully suggests that substantial additional amendments of claims **15 and 16** remain in order herein in order to adequately define the metes and bounds of the process(es) intended to be claimed therein.

Applicant’s amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a).

A shortened statutory period for response to this final action is set to expire **THREE MONTHS** from the date of this action. In the event a first response is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than **SIX MONTHS** from the date of this final action.

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner’s computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status Information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see < <http://pair-direct.uspto.gov> >. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

LECrane:lec
02/12/2010

/Lawrence E. Crane/

Primary Examiner, Art Unit 1623

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